Remarks

Claim Amendments

Claims 1-34 are pending. Claims 13-23 are amended to recite a process rather than a use. Claims 13 and 24 are amended to recite that one end of the strip is attached to the ventricle of a heart and the other end is attached to the atrium of the heart. Support for these amendments is found in the application at, for example, page 4, lines 16-24. Claim 24 is amended to recite "wherein said tract is prepared by a process." Support is found in the application at, for example, page 8, lines 5-15. Claims 12 and 34 are amended to correct typographical errors. These amendments are made without prejudice and do not introduce new matter.

Restriction Requirement

The restriction requirement divides the claims into the following groups:

Group 1, claims 1-12, drawn to a method of creating an atrioventricular bypass tract for a heart.

Group 2, claims 13-23, drawn to a method of use of mesenchymal stem cells.

Group 3, claims 24-34, drawn to an atrioventricular bypass tract for a heart.

Election with Traverse

In response to the restriction requirement of May 18, 2009, Applicants elect with traverse the following invention: Group 1.

Traversal

Applicants traverse the restriction requirement. The Examiner has based the restriction requirement on the alleged obviousness of the special technical feature of the claims over the prior art. Specifically, according to the Examiner, "[t]he special technical feature of creating an atrioventricular bypass of instant claims is unpatentable over Taheri et al (US Patent No. 6,690,970) in view of Pittenger et al (US patent No. 6,387,369)." According to the Examiner, there is no unity of invention because allegedly there is no special technical feature claimed, i.e., no feature that defines a contribution over the prior art.

Applicants traverse on the grounds that creating an atrioventricular bypass tract as recited in the pending claims is not obvious over the cited references. In this regard, it should be noted that the pending claims more particularly recite that the atrioventricular ("AV") bridge is created by "growing mesenchymal stem cells into a strip" and "attaching one end of the strip onto the atrium of the heart" while the other end of the strip is attached to "the ventricle of the heart," so that electrical signals generated by the sinus node can be propagated across the tract to excite the ventricle. As made clear in the specification (*see, e.g.*, application at 3), the tract serves to take over and "bypass" a diseased AV node. Hence, the recited bridge is created by attaching the strip to healthy atrium and ventricle tissue at each end, bypassing the damaged AV node. Applicants submit that the claim-recited method of creating a bridge is not taught or suggested by the cited art.

The claimed method clearly departs from any procedure disclosed by Taheri for treating AV block. As indicated, the claimed method entails growing a strip of cells *in vitro*, then implanting the strip of cells in the heart by attaching one end of the strip to healthy tissue in the atrium and attaching the other end to healthy tissue in the ventricle, bypassing the damaged AV node. In contrast, Taheri teaches implanting cells in <u>damaged</u> tissue in the heart and permitting the cells to proliferate outward to establish a connection between the atrium and the ventricle. *See, e.g.*, Taheri at col. 6, ll. 8-10 (referring to "[a]n implantation catheter **60** for mapping the block site **30** and injecting the implantation cells **26** therein") and at col. 5, ll. 59-60 ("the implantation cells **26** grow to form a conductive cell bridge **50**"). The Examiner expressly concedes that Taheri's procedure entails implanting cells at the AV node. *See* Office Action at 2.

Pittenger does not compensate for the deficiencies in Taheri. The Examiner concedes that Taheri "does not teach culturing the cells in strips," and therefore differs from the claims. Office Action at 2. The Examiner nonetheless asserts that Pittenger compensates for the deficiency by teaching the administration of mesenchymal stem cells to the heart "as a liquid injectable or as a preparation of cells in a matrix which is or becomes solid or semi-solid (see abstract). The reference teaches the use of liquid cell treatment and matrix cell support treatments." *Id.* at 2-3. "[T]herefore, it can be formed into strips that mimic the size of the ventricular valve, thus would allow ingrowth of the appropriate host cells and renewal of tissue over time (see column 1, lines 26-30)." *Id.* at 3.

Pittenger fails to remedy the deficiencies of Taheri. Taheri would only lead one to implant cells in damaged tissue, providing at most an outgrowth of cells to atrium and ventricle, which is distinct from attaching a bridge to healthy tissue as in the claim-recited method, as noted above. Pittenger seeks to regenerate or renew damaged tissue, not bypass it, and therefore at most only leads to placing the cells in the AV node, not across it. *See, e.g.*, Pittenger at col. 1, ll. 60-64 (outlining procedure that entails implanting MSC "into the damaged heart" and "in situ formation of myocardium"). Thus, neither reference teaches or suggests attaching a strip of cells to healthy tissue on both sides of damaged tissue to bypass the damaged tissue, as recited by the pending claims.

Two additional points undermine the Examiner's assertion that there would be a motivation to combine Pittenger with Taheri, and therefore also undermine the Examiner's contention that the present method of preparing a bypass bridge is unpatentable over the cited patents. First, the only passage of Pittenger specifically cited by the Examiner discusses a valve. Any discussion of a valve, however, is irrelevant to the present invention, which provides an AV bridge, not a valve. Such a bridge permits conduction of electrical signals from the atrium to the ventricle (*see* application as published ¶ 0012), and is therefore wholly distinct in structure and function from a valve, which permits blood to flow from one heart chamber to the next. *See, e.g.*, Arnold M. Katz, Physiology of the Heart 3-10 and 9 Figure 1-6 (4th ed. 2006) (diagram of heart illustrating tricuspid valve as wholly separate from AV node and AV bundle) (Exhibit A). Second, Applicants respectfully point out that, contrary to the Examiner's understanding, Pittenger does not "teach producing an atrioventricular bypass tract." Office Action at 3. The Examiner fails to identify any such teaching in Pittenger, nor does the Applicant see any.

Applicants also point out that the claimed bypass bridge is grown in vitro and then placed into the heart, one end attached to the atrium and one end attached to the ventricle, without the need for further cell proliferation or differentiation. In contrast, Taheri teaches implantation of cells into the heart that *subsequently grow in situ* to compensate for damaged or absent structures (*see, e.g.*, Taheri at col. 3, ll. 7-10 ("The implantation cells grow to form a conductive cell bridge around the malfunction area.")) and Pittenger teaches implantation of cells that differentiate and/or proliferate in order to provide otherwise missing or damaged structures (*see, e.g.*, Pittenger at col. 1, ll. 45-46 ("[t]he MSCs differentiate into cardiac muscle cells") and at col. 2, ll. 41-45 (the matrix "enhances the opportunity for the

administered MSCs to proliferate, differentiate and eventually become fully developed cardiomyocytes")).

In view of these distinctions over the asserted publications, Applicants traverse the restriction requirement.

Restriction of Connexins Cx43, Cx40, and Cx45

The Examiner has further required election of one of Cx43, Cx40, and Cx45. According to the Examiner, unity of invention is lacking because "Different gene: different due to different nucleotide sequences; Different connexins: due to different amino acid content: for example, connexin 40, connexin 43, or connexin 45." Applicants elect a nucleic acid that encodes Cx43 and the corresponding polypeptide encoded by a nucleic acid that encodes Cx43. Claims 1-7, 9, 11-18, 20, 22-29, 31, and 33-34 read on the elected species.

Conclusion

It is respectfully submitted that the presently pending claims are allowable. All issues raised by the Examiner having been addressed, an early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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